AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application. Applicant reserves the right for all the cancelled claims.

LISTING OF CLAIMS:

Claims 1-33 (cancelled)

34. (currently amended) A process for detoxifying bacterial lipopolysaccharide in a patient with septicemia caused by gram-negative bacteria, by gram-positive bacteria, by trauma or by injury, which comprises ~~the steps of determining an effective amount of lipopolysaccharide binding protein needed for detoxifying bacterial lipopolysaccharide in said patient wherein said effective amount of lipopolysaccharide binding protein elevates the concentration of lipopolysaccharide binding protein in said patient to a sufficiently high level to suppress lipopolysaccharide induced release of cytokine, and~~ administering to said patient in need ~~therefor said~~ an effective amount of lipopolysaccharide binding protein to elevate the serum concentration of lipopolysaccharide binding protein in said patient to a sufficiently high level to suppress lipopolysaccharide induced release of cytokine, thereby detoxifying the bacterial lipopolysaccharide.

35. The process of claim 34 wherein said lipopolysaccharide binding protein is a native or a recombinant lipopolysaccharide binding protein.

36. The process of claim 34, wherein said lipopolysaccharide binding protein is of human, rabbit, murine or rat lipopolysaccharide binding protein.

37. (Withdrawn) The process of claim 34, wherein said suppression of lipopolysaccharide-induced release of cytokine by lipopolysaccharide binding protein is enhanced by increasing the binding affinity of said lipopolysaccharide binding protein by means of mutation or hybridization.

38. (Currently amended) The process of claim 34, wherein said ~~concentration~~ serum concentration of lipopolysaccharide binding protein is ~~elevated to at least 4~~ from 15 to 275 μg/mL.

39. (currently amended) The process of claim ~~38~~ 34, wherein said serum concentration of lipopolysaccharide binding protein after administering thereof is ~~elevated to at least 10~~ from 50 to 275 μg/mL.

40. (currently amended) The process of claim 34~~39~~, wherein said serum concentration of lipopolysaccharide binding protein after administering thereof is ~~elevated to at least 20~~ from 100 to 257 μg/mL.

41. (withdrawn) A process for preventing toxification of bacterial lipopolysaccharide in a subject at risk of exposure to gram-negative bacteria or gram-positive bacteria, which comprises determining an effective amount of lipopolysaccharide binding protein needed for preventing toxification of bacterial lipopolysaccharide in said subject wherein said effective amount of lipopolysaccharide binding protein elevates the concentration of lipopolysaccharide binding protein in said subject to a sufficiently high level to prevent lipopolysaccharide-induced release of cytokine, and administering to said subject in need therefor said effective amount of lipopolysaccharide binding protein to elevate the concentration of lipopolysaccharide binding protein in said subject to a sufficiently high level to prevent lipopolysaccharide-induced release of cytokine.

REMARKS/ARGUMENTS

Claims 34-36, and 38-40 remain in the application. Claims 37 and 41 are withdrawn.

Claim Rejections under 35 USC § 102

The previous rejection of claims 34-41 under 35 USC § 102(b) as being anticipated by Scott et al. was withdrawn. The applicant thanks the examiner for her consideration of the applicant's response.

Claim Rejections under 35 USC § 102 & 103

The previous rejection of claims 34-41 under 35 USC § 102 & 103 as being anticipated by, or in the alternative, under 35 U.S.C. 103(a) as being obvious over Scott et al. was withdrawn. Applicant thanks the examiner for her consideration of applicant's response.

Claim Rejections under 35 USC § 112, First and second Paragraph

In vitro and in vivo correlation between human and murine sepsis models.

Claims 34-36, and 38-40 were rejected under 35 U.S.C. 112, first and second paragraph. The Examiner contends that the method of detoxifying bacterial lipopolysaccharide is enabling in mice, but may not be enabled for a human patient with septicemia due to lack of working example for human.

In response, applicant believes that Figures 1 to 7 provided working examples for the mouse *in vitro* and *in vivo* sepsis models. Further, the correlations between the molecular structures, the binding affinity, and the responses of human, rat, rabbit, and mouse LBPs to LPS were known in the prior art before the filing date of this application.

For example, the publications by Schumann et al. (Science Vol. 249, September 1990, 1429-1431), Su et al. (Journal of Immunology, 1994, 743-752), and Lengacher et al. (J. of inflammation, 47, 165-172, 1995/1996) demonstrate that LBP is a highly conserved protein, and that the LBP proteins of rat, rabbit, murine, and human share a high degree of homology. These

references also show that there are conserved peptide sequences in all of the LBP proteins that bind to the lipid A region of LPS. Lengacher et al's study also shows essentially the same binding property of human and murine LBPs to bacterial LPS. Therefore, LBPs of all species share similar capacity of LPS binding. Gazzano et al. (in Infection and immunity, April, 1994, 1185-1191) and Su et al. (Journal of Immunology, 1994, 743-752) show that rabbit LBP and human rLBP not only have similar binding affinity to LPS, but also response to bacterial LPS with similar level of acute phase LBP concentration.

Thus, it was well-known that a correlation exists between *in vitro* and *in vivo* animal sepsis models and human sepsis.

The published results of clinical trial by applicant confirmed the claimed invention

Applicant respectfully submits herein the published clinical studies by applicant to support applicant's position that the process of detoxifying bacterial lipopolysaccharide in a human patient with septicemia disclosed in the present application is adequately described and fully enabled.

A clinical study of 63 human patients with severe sepsis, published by Schumann et al in Blood, Volume 98, Number 13, December 2001, demonstrates the effectiveness of the process of detoxifying bacterial lipopolysaccharide in a human patient by injecting LBP protein to suppress bacterial LPS. First, in this study the patients showed an acute phase of LBP concentration ranging between 3.74 to 275 μg/mL (equivalent to mg/L, see results section under Serum LBP concentration in Severe Sepsis or Septic Shock). This result confirms the correlation between human and murine sepsis models previous published by Gazzano et al. (in Infection and immunity, April, 1994, 1185-1191) and by Su et al. (Journal of Immunology, 1994, 743-752). This study is also consistent with the *in vitro and in vivo* murine sepsis models illustrated in Figures 1 to 7 of the present invention. Second, the study demonstrates the effective inhibition of LPS by LBP in 63 patients with severe cases of sepsis (see Figures 7-8).

Claims 38-40 as amended are directed to dosage range disclosed in figures 1-4 of the application, as confirmed in Schumann et al.'s publication in Blood, Volume 98, Number 13, December 2001

(see Figures 7-8). Support for the claimed range was discussed above. Given this range of dosage, the result of this clinical study has adequately verified the dosage range of the claimed invention and thus confirms the operability of the presently claimed invention. Therefore, the claimed invention is disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

Based on the foregoing amendments and remarks, applicant respectfully requests withdrawal of these rejections.

Conclusion:

Based on the foregoing amendments and remarks, favorable consideration and allowance of all of the claims now present in the application are respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawings be further amended or corrected in formal respects in order to place the case in condition for final allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing this case to allowance, the Examiner is invited to telephone the undersigned.

The Commissioner is authorized to charge any required fees, including any extension and/or excess claim fees, any additional fees, or credit any overpayment, to Goodwin Procter LLP Deposit Account No. 06-0923.

Respectfully submitted for Applicant,

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